Chemical Abstracts

09/926,693 C Florence since 2/19/03 June 11, 2002

=> d que l7

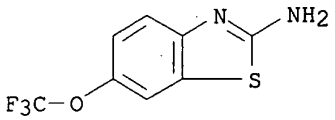
L1	1	SEA	FILE=REGISTRY	ABB=ON PLU=ON	RILUZOLE/CN
L2	5529	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	"MULTIPLE SCLEROSIS"/CT
L3	260	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	L1
L4	3	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	L2 AND L3
L5	157	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	L1(L)THU/RL
L6	3	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	L2 AND L5
L7	3	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	L4 OR L6

L7 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:923612 HCAPLUS
DN 136:42875
TI Pharmaceutical composition containing Riluzole for the treatment of multiple sclerosis
IN Melamed, Eldad; Ophen, Daniel
PA Mor - Research Applications Ltd., Israel
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001095907	A1	20011220	WO 2001-IL534	20010612

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI IL 2000-136687 A 20000612
AB An oral pharmaceutical compn. for the treatment of multiple sclerosis (MS) comprises a pharmaceutically acceptable carrier and as an active ingredient, Riluzole. Riluzole, a drug that inhibits glutamatergic release, is shown to be effective in the prevention and treatment of MS. The effect of Riluzole is shown in an animal model of MS, an exptl. autoimmune encepthalomyelitis (EAE) model produced by injection of myelin oligodendrocyte glycoprotein (MOG) to animals. Administration of Riluzole to such animals before they develop the MS-related symptoms markedly reduced the incidence and clin. severity of the disease in such animals. Moreover, treatment of such animals after the appearance of severe MS-related symptoms, also markedly slowed down the progression of the disease and improved the clin. manifestations.
IT **1744-22-5**, Riluzole
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(oral compn. contg. Riluzole for treatment of multiple sclerosis)
RN 1744-22-5 HCAPLUS
CN 2-Benzothiazolamine, 6-(trifluoromethoxy)- (9CI) (CA INDEX NAME)



IC ICM A61K031-428
ICS A61P025-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

ST Riluzole oral multiple sclerosis
IT Glycoproteins
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(MOG (myelin-oligodendroglial glycoprotein); oral compn. contg. Riluzole for treatment of multiple sclerosis in MOG-induced autoimmune encephalomyelitis as animal model)
IT Encephalomyelitis
(autoimmune; oral compn. contg. Riluzole for treatment of multiple sclerosis in autoimmune encephalomyelitis as animal model)
IT Disease models
(oral compn. contg. Riluzole for treatment of multiple sclerosis in autoimmune encephalomyelitis as animal model)
IT Drug delivery systems
(oral; oral compn. contg. Riluzole for treatment of multiple sclerosis)
IT **Multiple sclerosis**
(therapeutic agents; oral compn. contg. Riluzole for treatment of multiple sclerosis)
IT **1744-22-5**, Riluzole
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(oral compn. contg. Riluzole for treatment of multiple sclerosis)
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

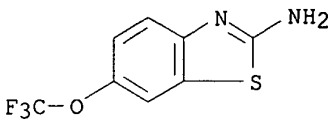
L7 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:880959 HCAPLUS
DN 134:25377
TI Use of riluzole for the treatment of multiple sclerosis
IN Polman, Chris
PA Vereniging Voor Christelijk Wetenschappelikjk Onderwijs, Neth.; Biogen, Inc.
SO PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000074676	A1	20001214	WO 2000-IB933	20000602
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1187612	A1	20020320	EP 2000-939007	20000602
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRAI EP 1999-201788 A 19990604
US 2000-174328P P 20000104
WO 2000-IB933 W 20000602

AB Methods and compns. are provided for the treatment of multiple sclerosis with riluzole [6-(trifluoromethoxy)-benzothiazolamine].
IT **1744-22-5**, Riluzole

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(riluzole for multiple sclerosis treatment)
RN 1744-22-5 HCAPLUS
CN 2-Benzothiazolamine, 6-(trifluoromethoxy)- (9CI) (CA INDEX NAME)



IC ICM A61K031-425
CC 1-11 (Pharmacology)
Section cross-reference(s): 63
ST riluzole multiple sclerosis
IT Drug delivery systems
(riluzole for multiple sclerosis treatment)
IT **Multiple sclerosis**
(therapeutic agents; riluzole for multiple sclerosis treatment)
IT Interferons
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.1, .beta.1a and .beta.1b; riluzole for multiple sclerosis treatment)
IT **1744-22-5**, Riluzole 147245-92-9, Copaxone
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(riluzole for multiple sclerosis treatment)
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:640417 HCAPLUS
DN 129:239904
TI Method of evaluating the efficacy of drug on brain nerve cells using measurement of N-acetylaspartate with magnetic resonance spectroscopy
IN Arnold, Douglas L.; Cashman, Neil; Kalra, Sanjay
PA Can.
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9841882	A1	19980924	WO 1998-CA230	19980313

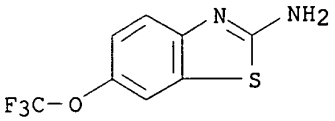
W: CA, US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRAI CA 1997-2200045 19970314
AB A method is provided for measurement in vivo of the effect of a drug on the function of the nerve cells of the brain of a patient suffering from a

neurol. disease. The method comprises (a) measuring N-acetylaspartate (NAA) signal intensity using magnetic resonance spectroscopy (MRS) of the brain of the patient; (b) subjecting the patient to a treatment with the drug to be tested and measuring NAA signal intensity using MRS of the brain of the patient; and (c) comparing the spectra of steps (a) and (b) to det. whether the drug has an effect on the function of the nerve cells of the brain. An increase in the NAA signal of step (b) is indicative of a drug with a pos. effect.

IT **1744-22-5**, Riluzole
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(evaluation of efficacy of drugs on brain nerve cells using measurement of acetylaspartate with magnetic resonance spectroscopy)

RN 1744-22-5 HCAPLUS

CN 2-Benzothiazolamine, 6-(trifluoromethoxy)- (9CI) (CA INDEX NAME)



IC ICM G01R033-483

CC 1-11 (Pharmacology)
Section cross-reference(s): 8

ST drug effect brain disorder acetylaspartate MRS; magnetic resonance spectroscopy acetylaspartate brain disorder; neuron brain magnetic resonance spectroscopy acetylaspartate

IT Imaging
(NMR; evaluation of efficacy of drugs on brain nerve cells using measurement of acetylaspartate with magnetic resonance spectroscopy)

IT Nervous system
(amyotrophic lateral sclerosis; evaluation of efficacy of drugs on brain nerve cells using measurement of acetylaspartate with magnetic resonance spectroscopy)

IT Nervous system
(degeneration; evaluation of efficacy of drugs on brain nerve cells using measurement of acetylaspartate with magnetic resonance spectroscopy)

IT Nervous system
(disease; evaluation of efficacy of drugs on brain nerve cells using measurement of acetylaspartate with magnetic resonance spectroscopy)

IT Anti-Alzheimer's agents
Anticonvulsants
Brain
Multiple sclerosis
Nervous system agents
(evaluation of efficacy of drugs on brain nerve cells using measurement of acetylaspartate with magnetic resonance spectroscopy)

IT Spectroscopy
(magnetic resonance; evaluation of efficacy of drugs on brain nerve cells using measurement of acetylaspartate with magnetic resonance spectroscopy)

IT Nerve

(neuron; evaluation of efficacy of drugs on brain nerve cells using measurement of acetylaspartate with magnetic resonance spectroscopy)

IT Brain, disease
(stroke; evaluation of efficacy of drugs on brain nerve cells using measurement of acetylaspartate with magnetic resonance spectroscopy)

IT **1744-22-5**, Riluzole 2156-56-1, Sodium dichloroacetate 30516-87-1, Zidovudine 60142-96-3, Gabapentin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(evaluation of efficacy of drugs on brain nerve cells using measurement of acetylaspartate with magnetic resonance spectroscopy)

IT 57-00-1, Creatine 997-55-7
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(evaluation of efficacy of drugs on brain nerve cells using measurement of acetylaspartate with magnetic resonance spectroscopy)

MEDLINE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=> d que
L9          275 SEA FILE=MEDLINE ABB=ON  PLU=ON  RILUZOLE/CT
L10       20258 SEA FILE=MEDLINE ABB=ON  PLU=ON  MULTIPLE SCLEROSIS+NT/CT
L11           1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L9 AND L10
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L11 ANSWER 1 OF 1 MEDLINE
ACCESSION NUMBER: 1999424113 MEDLINE
DOCUMENT NUMBER: 99424113 PubMed ID: 10494326
TITLE: [New therapies in neurology, but who benefits?]. Nieuwe therapieen in de neurologie, maar wie wordt er beter van?.
AUTHOR: Vermeulen M; de Haan R J
CORPORATE SOURCE: Afd. Neurologie, Academisch Medisch Centrum, Amsterdam.
SOURCE: NEDERLANDS TIJDSCHRIFT VOOR GENEESKUNDE, (1999 Aug 28) 143 (35) 1764-6. Ref: 11
Journal code: 0400770. ISSN: 0028-2162.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Dutch
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991029

AB In recent years several new treatments have been introduced in neurology, sumatriptan in migraine, riluzole in amyotrophic lateral sclerosis, interferon-beta in multiple sclerosis and rivastigmine in Alzheimer's disease. Doubts exist on the effects on functional outcome of these new treatments. Hardly effective drugs are not forced on physicians by the pharmaceutical industry, since physicians are involved in decisions from phase I studies to the final approval of the drugs. The problem is, however, that in clinical studies emphasis is still on statistically significant differences rather than on meaningful differences in the functional status of patients. In conclusion, in clinical studies outcome measures should be chosen more carefully and there is a need for sensitive linear functional scales.

CT Check Tags: Human
Alzheimer Disease: DT, drug therapy
Amyotrophic Lateral Sclerosis: DT, drug therapy
Antiviral Agents: TU, therapeutic use
Carbamates: TU, therapeutic use
English Abstract
Interferon-beta: TU, therapeutic use
Migraine: DT, drug therapy
Multiple Sclerosis: DT, drug therapy
*Nervous System Diseases: DT, drug therapy
Netherlands
Neuroprotective Agents: TU, therapeutic use
*Outcome Assessment (Health Care): MT, methods
Riluzole: TU, therapeutic use
Sumatriptan: TU, therapeutic use
Vasoconstrictor Agents: TU, therapeutic use

RN 103628-46-2 (Sumatriptan); 123441-03-2 (rivastigmine); 1744-22-5 (Riluzole); 77238-31-4 (Interferon-beta)
CN 0 (Antiviral Agents); 0 (Carbamates); 0 (Neuroprotective Agents); 0 (Vasoconstrictor Agents)

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=> d que
L9          275 SEA FILE=MEDLINE ABB=ON  PLU=ON  RILUZOLE/CT
L14       71529 SEA FILE=MEDLINE ABB=ON  PLU=ON  SPINAL CORD?/CT
L15          18 SEA FILE=MEDLINE ABB=ON  PLU=ON  L9 AND L14
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L15 ANSWER 1 OF 18 MEDLINE
ACCESSION NUMBER: 2001229774 MEDLINE
DOCUMENT NUMBER: 21196980 PubMed ID: 11302627
TITLE: Evaluation of the neuroprotective effects of sodium channel blockers after spinal cord injury: improved behavioral and neuroanatomical recovery with riluzole.
AUTHOR: Schwartz G; Fehlings M G
CORPORATE SOURCE: Division of Cell and Molecular Biology, The Toronto Western Research Institute, Ontario, Canada.
SOURCE: JOURNAL OF NEUROSURGERY, (2001 Apr) 94 (2 Suppl) 245-56. Journal code: 0253357. ISSN: 0022-3085.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010502
Last Updated on STN: 20010502
Entered Medline: 20010426

AB OBJECT: Persistent activation of voltage-sensitive Na+ channels is associated with cellular toxicity and may contribute to the degeneration of neural tissue following traumatic brain and spinal cord injury (SCI). Pharmacological blockade of these channels can attenuate secondary pathophysiology and reduce functional deficits acutely. METHODS: To determine the therapeutic effects of Na+ channel blockers on long-term tissue sparing and functional neurological recovery after traumatic SCI, the authors injected Wistar rats intraperitoneally with riluzole (5 mg/kg), phenytoin (30 mg/kg), CNS5546A, a novel Na+ channel blocker (15 mg/kg), or vehicle (2-HP3CD; 5 mg/kg) 15 minutes after induction of compressive SCI at C7-T1. Functional neurological recovery of coordinated hindlimb function and strength, assessed 1 week postinjury and weekly thereafter for 6 weeks, was significantly enhanced in animals treated with riluzole compared with the other treatment groups. Seven weeks postinjury the preservation of residual tissue and integrity of descending axons were determined with digital morphometrical and fluorescent histochemical analysis. All three Na+ channel blockers significantly enhanced residual tissue area at the injury epicenter compared with control. Riluzole significantly reduced tissue loss in rostrocaudal regions surrounding the epicenter, with overall sparing of gray matter and selective sparing of white matter. Also, counts of red nuclei neurons retrogradely labeled with fluorogold introduced caudal to the injury site were significantly increased in the riluzole group. CONCLUSIONS: Systemic Na+ channel blockers, in particular riluzole, can confer significant neuroprotection after in vivo SCI and result in behavioral recovery and sparing of both gray and white matter.

CT Check Tags: Animal; Female; Support, Non-U.S. Gov't
Axons: DE, drug effects
Axons: PA, pathology
Behavior, Animal: DE, drug effects
Efferent Pathways: DE, drug effects
Efferent Pathways: PA, pathology
*Neuroprotective Agents: TU, therapeutic use
Rats
Rats, Wistar
***Riluzole: TU, therapeutic use**
*Sodium Channel Blockers

Spinal Cord: DE, drug effects
Spinal Cord: PA, pathology
Spinal Cord: PP, physiopathology
Spinal Cord Compression: ET, etiology
Spinal Cord Injuries: CO, complications
***Spinal Cord Injuries: DT, drug therapy**
Spinal Cord Injuries: PA, pathology
Spinal Cord Injuries: PX, psychology
RN 1744-22-5 (Riluzole)
CN 0 (Neuroprotective Agents); 0 (Sodium Channel Blockers)

L15 ANSWER 2 OF 18 MEDLINE
ACCESSION NUMBER: 2001132615 MEDLINE
DOCUMENT NUMBER: 20575755 PubMed ID: 11135009
TITLE: The effect of riluzole treatment in rats on the survival of injured adult and grafted embryonic motoneurons.
AUTHOR: Nogradi A; Vrbova G
CORPORATE SOURCE: Department of Ophthalmology, Albert Szent-Gyorgyi Medical Centre, University of Szeged, 6720-SzegedKoranyi fasor 10-11, Hungary.. nogradi@poht.szote.u-szeged.hu
SOURCE: EUROPEAN JOURNAL OF NEUROSCIENCE, (2001 Jan) 13 (1) 113-8. Journal code: 8918110. ISSN: 0953-816X.
PUB. COUNTRY: France
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010301

AB The effect of riluzole on the survival of injured motoneurons was studied. The L4 ventral root was avulsed and reimplanted into the spinal cord. Immediately after the operation, 4 animals were treated with riluzole for 3 weeks while another 4 animals received no treatment after the operation. Three months later the fluorescent dyes, Fast Blue and Diamidino Yellow, were applied to the cut ventral ramus of the L4 spinal nerve, for retrograde labelling of neurons. Three days later, the spinal cords were processed to reveal the retrograde-labelled cells. In untreated animals, there were 20 +/- 2.1 labelled neurons (+/- SEM), while in animals treated with riluzole there were 723 +/- 26. Thus, treatment with riluzole dramatically enhanced the survival of injured motoneurons. In another series of experiments, after avulsion of the L4 ventral root and its reinsertion, embryonic spinal cord pieces were grafted into the host cord. Five animals received riluzole treatment and 4 were left untreated. In the untreated animals, 125 +/- 5.1 retrograde-labelled cells of both graft and host origin were detected. In rats treated with riluzole, 645 +/- 35.7 retrograde-labelled cells were seen and almost all of these were of host origin. Thus, treatment with riluzole enhanced the survival of injured host motoneurons, and by doing so, (i) reduced the ability of grafted neurons to extend their axons into the reimplanted L4 ventral root, and (ii) reduced the survival of the grafted cells.

CT Check Tags: Animal; Support, Non-U.S. Gov't
Cell Survival: DE, drug effects
Embryo
Motor Neurons: DE, drug effects
*Motor Neurons: PH, physiology
*Motor Neurons: TR, transplantation

Nerve Regeneration
*Neuroprotective Agents: PD, pharmacology
Rats
Rats, Wistar
*Replantation
***Riluzole: PD, pharmacology**
***Spinal Cord: SU, surgery**
*Spinal Nerve Roots: IN, injuries
Spinal Nerve Roots: PA, pathology
*Spinal Nerve Roots: PP, physiopathology
RN 1744-22-5 (Riluzole)
CN 0 (Neuroprotective Agents)

L15 ANSWER 3 OF 18 MEDLINE
ACCESSION NUMBER: 2001029518 MEDLINE
DOCUMENT NUMBER: 20500776 PubMed ID: 11046220
TITLE: Neuroprotective effects of riluzole and ketamine during transient spinal cord ischemia in the rabbit.
AUTHOR: Lips J; de Haan P; Bodewits P; Vanicky I; Dzoljic M; Jacobs M J; Kalkman C J
CORPORATE SOURCE: Academic Medical Center, University of Amsterdam, The Netherlands.
SOURCE: ANESTHESIOLOGY, (2000 Nov) 93 (5) 1303-11.
Journal code: 1300217. ISSN: 0003-3022.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001121

AB BACKGROUND: Massive release of central excitatory neurotransmitters is an important initial step in ischemic neuronal injury, and modification of this process may provide neuroprotection. We studied the protective effects of the voltage-dependent sodium channel antagonist riluzole and the N-methyl-d-aspartate receptor antagonist ketamine on hind limb motor function and histopathologic outcome in an experimental model of spinal cord ischemia. METHODS: Temporary spinal cord ischemia was induced by 29 min of infrarenal balloon occlusion of the aorta in 60 anesthetized New Zealand white rabbits. Animals were randomly assigned to one of four treatment groups (n = 15 each): group C, saline (control); group R, riluzole, 8 mg/kg intravenously; group K, ketamine, 55 mg/kg intravenously; group RK, riluzole and ketamine. After reperfusion, riluzole treatment was continued with intraperitoneal infusions. Normothermia (38 degrees C) was maintained during ischemia, and rectal temperature was assessed before and after intraperitoneal infusions. Neurologic function, according to Tarlov's criteria, was evaluated every 24 h, and infarction volume and the number of eosinophilic neurons and viable motoneurons in the lumbosacral spinal cord was evaluated after 72 h. RESULTS: Neurologic outcome was better in groups R and RK than in groups C and K. All animals in group C (100%) and all animals but one in group K (93%) were paraplegic 72 h after the ischemic insult versus 53% in group R and 67% in group RK ($P < 0.01$ each). More viable motoneurons were present in groups R and RK than in controls ($P < 0.05$). CONCLUSIONS: The data indicate that treatment with riluzole can increase the tolerance of spinal cord motoneurons to a period of normothermic ischemia.

Intraischemic ketamine did not provide neuroprotection in this model.

CT Check Tags: Animal; Comparative Study; Support, Non-U.S. Gov't
Disease Models, Animal
Excitatory Amino Acid Antagonists: PD, pharmacology
Infarction: ET, etiology
Infarction: PA, pathology
Infarction: PC, prevention & control
*Ketamine: PD, pharmacology
*Neuroprotective Agents: PD, pharmacology
Paraplegia: ET, etiology
Paraplegia: PC, prevention & control
Rabbits
***Riluzole: PD, pharmacology**
Spinal Cord: BS, blood supply
Spinal Cord: PA, pathology
Spinal Cord Ischemia: CO, complications
***Spinal Cord Ischemia: DT, drug therapy**

RN 1744-22-5 (Riluzole); 6740-88-1 (Ketamine)

CN 0 (Excitatory Amino Acid Antagonists); 0 (Neuroprotective Agents)

L15 ANSWER 4 OF 18 MEDLINE

ACCESSION NUMBER: 2000470324 MEDLINE

DOCUMENT NUMBER: 20359137 PubMed ID: 10899284

TITLE: Riluzole increases high-affinity glutamate uptake in rat spinal cord synaptosomes.

AUTHOR: Azbill R D; Mu X; Springer J E

CORPORATE SOURCE: Department of Anatomy and Neurobiology, Spinal Cord and Brain Injury Research Center, University of Kentucky Medical Center, Lexington, KY 40536-0084, USA.

CONTRACT NUMBER: NS-30248 (NINDS)

SOURCE: BRAIN RESEARCH, (2000 Jul 21) 871 (2) 175-80.
Journal code: 0045503. ISSN: 0006-8993.

PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200010

ENTRY DATE: Entered STN: 20001012
Last Updated on STN: 20001012
Entered Medline: 20001004

AB The purpose of this study was to examine the effect of the anti-convulsant agent, riluzole, on high-affinity glutamate uptake as measured in rat spinal cord synaptosomes. The rate of glutamate uptake was significantly increased in the presence of 0.1 microM and 1.0 microM riluzole, but not at the higher concentrations examined. Kinetics analysis demonstrated that riluzole (0.1 microM) decreased the apparent K(m) by 21% and increased the V(max) by 31%. Glutamate uptake also was significantly increased in spinal cord synaptosomes obtained from rats treated with 8 mg/kg (i.p.) of riluzole and sacrificed 4 h later. The increase in glutamate uptake in vitro was not affected by pretreatment either with H7, an inhibitor of PKA and PKC, or with the PKC activating phorbol ester, 12-O-tetradecanoylphorbol 13-acetate. Previous studies have shown that some of the actions of riluzole are mediated by G proteins sensitive to pertussis toxin. Surprisingly, treatment of synaptosomes with pertussis toxin alone increased the rate of glutamate uptake, while having no effect on uptake in the presence of riluzole. However, pretreatment with cholera toxin was found to completely block the effects of riluzole on glutamate uptake.

These results reveal an additional mechanism by which riluzole can affect glutamatergic neurotransmission, and provides further support that riluzole may prove beneficial in the treatment of traumatic central nervous system injuries involving the excitotoxic actions of glutamate.

CT Check Tags: Animal; Female; Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*ATP-Binding Cassette Transporters: DE, drug effects
*ATP-Binding Cassette Transporters: ME, metabolism
Amino Acid Transport System X-AG
Dose-Response Relationship, Drug
GTP-Binding Proteins: DE, drug effects
GTP-Binding Proteins: ME, metabolism
*Glutamic Acid: ME, metabolism
Rats
Rats, Long-Evans
***Riluzole: PD, pharmacology**
Signal Transduction: DE, drug effects
Signal Transduction: PH, physiology
***Spinal Cord: DE, drug effects**
Spinal Cord: ME, metabolism
Spinal Cord: UL, ultrastructure
*Synaptosomes: DE, drug effects
Synaptosomes: ME, metabolism
Synaptosomes: UL, ultrastructure
RN 1744-22-5 (Riluzole); 56-86-0 (Glutamic Acid)
CN 0 (ATP-Binding Cassette Transporters); 0 (Amino Acid Transport System X-AG); EC 3.6.1.- (GTP-Binding Proteins)

L15 ANSWER 5 OF 18 MEDLINE
ACCESSION NUMBER: 2000469184 MEDLINE
DOCUMENT NUMBER: 20384315 PubMed ID: 10925226
TITLE: Ischemic spinal cord injury induced by aortic cross-clamping: prevention by riluzole.
AUTHOR: Lang-Lazdunski L; Heurteaux C; Mignon A; Mantz J; Widmann C; Desmonts J; Lazdunski M
CORPORATE SOURCE: Department of Cardiovascular Surgery, Hopital Bichat and Xavier Bichat Medical University, Paris, France.. loic.lang@wanadoo.fr
SOURCE: EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY, (2000 Aug) 18 (2) 174-81.
Journal code: 8804069. ISSN: 1010-7940.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 20001012
Last Updated on STN: 20001012
Entered Medline: 20001003

AB OBJECTIVE: Recent studies confirmed the deleterious role of glutamate in the pathophysiology of spinal cord ischemia induced by aortic cross-clamping. We investigated the effect of riluzole, an anti-glutamate drug, in a rat model of spinal cord ischemia. MATERIALS AND METHODS: Spinal cord ischemia was induced in normothermia for 14 min in Sprague-Dawley rats using direct aortic arch plus left subclavian artery cross-clamping through a limited thoracotomy. Experimental groups were as follows: sham-operation (n=15), control (n=15) receiving only vehicle,

riluzole (n=15) receiving riluzole (4 mg/kg) before clamping and at the onset of reperfusion. Separate animals were used for monitoring physiologic parameters in the sham-operation (n=3), control (n=5), and riluzole (n=5) groups. Neurologic status was assessed at 6, 24 h, and then daily up to 96 h. Rats were randomly killed at 24, 48, or 96 h (n=5 for each time). Spinal cords were harvested for histopathology, immunohistochemistry for microtubule-associated protein 2 (MAP-2), TUNEL staining, and analysis of DNA fragmentation by agarose gel electrophoresis. RESULTS: All sham-operated rats had a normal neurologic outcome, whereas all control rats suffered severe and definitive paraplegia. Riluzole-treated rats had significantly better neurologic function compared to the control. Histopathology disclosed severe neuronal necrosis in the lumbar gray matter of control rats, whereas riluzole-treated rats suffered usually mild to moderate injury. Riluzole particularly prevented motor neurons injury. MAP-2 immunoreactivity was completely lost in control rats, whereas it was preserved either completely or partly in riluzole-treated rats. TUNEL staining revealed numerous apoptotic neurons scattered within the whole gray matter of control rats. Riluzole prevented or dramatically attenuated apoptotic neuronal death in treated rats. DNA extracted from lumbar spinal cords of sham-operated and riluzole-treated rats exhibited no laddering, whereas spinal cords from control rats showed DNA laddering with fragmentation into approximately 180 multiples of base pairs. CONCLUSIONS: Riluzole may protect the spinal cord in a setting of severe ischemia by preventing neuronal necrosis and apoptosis. This drug may therefore be considered for clinical use during 'high risk' surgical procedures on the thoracoabdominal aorta.

CT Check Tags: Animal; Comparative Study; Male; Support, Non-U.S. Gov't
Aorta, Thoracic: SU, surgery
Apoptosis: DE, drug effects
Biological Markers
Electrophoresis, Agar Gel
*Excitatory Amino Acid Antagonists: TU, therapeutic use
In Situ Nick-End Labeling
Ligation: AE, adverse effects
Microtubule-Associated Proteins: ME, metabolism
Necrosis
Neurons: ME, metabolism
Neurons: PA, pathology
Rats
Rats, Sprague-Dawley
Riluzole: TU, therapeutic use
Spinal Cord: ME, metabolism
***Spinal Cord: PA, pathology**
Spinal Cord Ischemia: ET, etiology
Spinal Cord Ischemia: ME, metabolism
Spinal Cord Ischemia: PA, pathology
***Spinal Cord Ischemia: PC, prevention & control**

RN 1744-22-5 (Riluzole)

CN 0 (Biological Markers); 0 (Excitatory Amino Acid Antagonists); 0 (Microtubule-Associated Proteins)

L15 ANSWER 6 OF 18 MEDLINE
ACCESSION NUMBER: 2000453566 MEDLINE
DOCUMENT NUMBER: 20464412 PubMed ID: 11011817
TITLE: Riluzole and methylprednisolone combined treatment improves functional recovery in traumatic spinal cord injury.

AUTHOR: Mu X; Azbill R D; Springer J E
CORPORATE SOURCE: Department of Anatomy and Neurobiology, University of Kentucky Medical Center, Lexington 40536-0084,USA.
CONTRACT NUMBER: NS30248 (NINDS)
NS40015 (NINDS)
SOURCE: JOURNAL OF NEUROTRAUMA, (2000 Sep) 17 (9) 773-80.
Journal code: 8811626. ISSN: 0897-7151.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010201

AB The potential use of riluzole (a glutamate release inhibitor) alone or in combination with methyl-prednisolone (MP) in treating acute spinal cored injury (SCI) was examined. Rats received a contusion injury to the spinal cord using the NYU impactor and were treated with vehicle, riluzole (8 mg/kg), MP(30 mg/kg), or riluzole + MP at 2 and 4 h following injury. Animals continued to receive riluzole treatment (8 mg/kg) for a period of 1 week. The animals were then tested weekly for functional recovery using the BBB open field locomotor score. At the end of testing (6 weeks after injury), each spinal cord was examined for the amount of remaining tissue at the injury site and a myelination index was used to quantify remaining axons in the ventromedial white matter. In this study, only the combination treatment was found to significantly improve behavioral recovery as assessed using the BBB open field locomotor scale. In addition, the combination treatment promoted tissue sparing at the lesion epicenter, but had no clear effect on the index of myelination. The results of this study clearly demonstrate the potential beneficial effects of a combination approach in the treatment of traumatic SCI.

CT Check Tags: Animal; Female; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Drug Therapy, Combination
*Excitatory Amino Acid Antagonists: PD, pharmacology
Gait Disorders, Neurologic: DT, drug therapy
Gait Disorders, Neurologic: PA, pathology
Gait Disorders, Neurologic: RH, rehabilitation
*Glucocorticoids, Synthetic: PD, pharmacology
Glutamic Acid: ME, metabolism
Locomotion: DE, drug effects
*Methylprednisolone: PD, pharmacology
Myelin Sheath: PA, pathology
Myelin Sheath: PH, physiology
Rats
Rats, Long-Evans
Recovery of Function: DE, drug effects
***Riluzole: PD, pharmacology**
Spinal Cord: DE, drug effects
Spinal Cord: ME, metabolism
Spinal Cord: PA, pathology
***Spinal Cord Injuries: DT, drug therapy**
Spinal Cord Injuries: PA, pathology
Spinal Cord Injuries: RH, rehabilitation
RN 1744-22-5 (Riluzole); 56-86-0 (Glutamic Acid); 83-43-2 (Methylprednisolone)

CN 0 (Excitatory Amino Acid Antagonists); 0 (Glucocorticoids, Synthetic)

L15 ANSWER 7 OF 18 MEDLINE
ACCESSION NUMBER: 2000401930 MEDLINE
DOCUMENT NUMBER: 20329773 PubMed ID: 10869502
TITLE: Riluzole improves measures of oxidative stress following traumatic spinal cord injury.
AUTHOR: Mu X; Azbill R D; Springer J E
CORPORATE SOURCE: Department of Anatomy and Neurobiology, Center for Spinal Cord and Brain Injury Research, University of Kentucky Medical Center, 800 Rose Street, Lexington, KY 40536-0084, USA.
CONTRACT NUMBER: NS-30248 (NINDS)
NS40015 (NINDS)
SOURCE: BRAIN RESEARCH, (2000 Jul 7) 870 (1-2) 66-72.
Journal code: 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000901
Last Updated on STN: 20000901
Entered Medline: 20000821

AB Rats received a contusion injury to the spinal cord followed by treatment with riluzole (a glutamate release inhibitor, 8 mg/kg), methylprednisolone (MP 30 mg/kg) or both. At 4 h following injury, spinal cords were removed and synaptosomes prepared and examined using five measures of oxidative stress. Riluzole treatment was found to improve mitochondrial function, and enhance glutamate and glucose uptake. As expected, MP treatment was found to reduce lipid peroxidation, but also improved glutamate and glucose uptake. Interestingly, the combination treatment was found to be effective in improving all five measures of oxidative stress. The results of this study clearly demonstrate the potential beneficial effects of a combination approach in the treatment of oxidative stress events in traumatic spinal cord injury.

CT Check Tags: Animal; Female; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Glutamic Acid: ME, metabolism
Glutamic Acid: TO, toxicity
Mitochondria: ME, metabolism
*Neuroprotective Agents: PD, pharmacology
Neurotoxins: ME, metabolism
*Oxidative Stress: DE, drug effects
Rats
Rats, Long-Evans
Rhodamines
***Riluzole: PD, pharmacology**
***Spinal Cord Injuries: DT, drug therapy**
***Spinal Cord Injuries: ME, metabolism**
Synaptosomes: ME, metabolism
Thiobarbituric Acid Reactive Substances: ME, metabolism
RN 109244-58-8 (dihydrorhodamine 123); 1744-22-5 (Riluzole); 56-86-0 (Glutamic Acid)
CN 0 (Neuroprotective Agents); 0 (Neurotoxins); 0 (Rhodamines); 0 (Thiobarbituric Acid Reactive Substances)

L15 ANSWER 8 OF 18 MEDLINE
ACCESSION NUMBER: 2000336784 MEDLINE
DOCUMENT NUMBER: 20336784 PubMed ID: 10876221
TITLE: Prevention of ischemic spinal cord injury: comparative effects of magnesium sulfate and riluzole.
AUTHOR: Lang-Lazdunski L; Heurteaux C; Dupont H; Widmann C; Lazdunski M
CORPORATE SOURCE: Departments of Cardiovascular Surgery and Anesthesiology, Hopital Bichat and Xavier Bichat Medical University, Paris, France.
SOURCE: JOURNAL OF VASCULAR SURGERY, (2000 Jul) 32 (1) 179-89. Journal code: 8407742. ISSN: 0741-5214.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000811
Last Updated on STN: 20000811
Entered Medline: 20000802

AB PURPOSE: Excitotoxic mechanisms have been implicated in the pathophysiology of spinal cord ischemic injury induced by aortic cross-clamping. We investigated the effects of the anti-excitotoxic drugs magnesium sulfate (MgSO(4)) and riluzole in a rabbit model of spinal cord ischemia. METHOD: The infrarenal aorta of New Zealand albino white rabbits (n = 68) was occluded for 40 minutes. Experimental groups included: a control group, which received only vehicle (n = 17); group A (n = 17), which received riluzole (8 mg/kg) before clamping; group B (n = 17), which received MgSO(4) (100 mg/kg) before clamping; and group C (n = 17), which received riluzole (8 mg/kg) and MgSO(4) (100 mg/kg) before clamping. Five additional rabbits had the same operation, but did not undergo aortic clamping (sham operation). The neurological status of the rabbits was assessed at 24 hours, 48 hours, and then daily for as long as 120 hours by using a modified Tarlov scale. The rabbits were killed at 24 hours (n = 3 per group), 48 hours (n = 4 per group), and 120 hours (n = 10 per group) postoperatively. Spinal cords were harvested for histopathologic and immunohistochemistry examinations for microtubule-associated protein-2 (MAP-2), a cytoskeletal protein specific from neurons. RESULTS: No major adverse effect was observed with either riluzole or MgSO(4). All control rabbits became severely paraplegic. All riluzole-treated and MgSO(4)-treated animals had a better neurological status than control animals. Typical morphological changes characteristic of neuronal necrosis in the gray matter of control animals was demonstrated by means of the histopathological examination, whereas riluzole or magnesium prevented or attenuated necrotic phenomenons. Moreover, MAP-2 immunoreactivity was completely lost in control rabbits, whereas it was preserved, either completely or partially, in rabbits treated with riluzole or magnesium. Riluzole was more effective than MgSO(4) in preventing paraplegia caused by motor neuron injury (P <.01). Riluzole and MgSO(4) had no additive neuroprotective effect. CONCLUSION: These results demonstrate that riluzole and, to a lesser extent, MgSO(4) may afford significant spinal cord protection in a setting of severe ischemia and may, therefore, be considered for clinical use during "high-risk" operations on the thoracic and thoracoabdominal aorta.

CT Check Tags: Animal; Comparative Study; Female; Support, Non-U.S. Gov't
Aorta
Aorta, Thoracic: SU, surgery

Constriction
Immunohistochemistry
*Ischemia: PC, prevention & control
*Magnesium Sulfate: TU, therapeutic use
Microtubule-Associated Proteins: ME, metabolism
*Neuroprotective Agents: TU, therapeutic use
Paraplegia: PC, prevention & control
Rabbits
*Receptors, N-Methyl-D-Aspartate: AI, antagonists & inhibitors
***Riluzole: TU, therapeutic use**
***Spinal Cord: BS, blood supply**
Treatment Outcome
RN 1744-22-5 (Riluzole); 7487-88-9 (Magnesium Sulfate)
CN 0 (Microtubule-Associated Proteins); 0 (Neuroprotective Agents); 0 (Receptors, N-Methyl-D-Aspartate)

L15 ANSWER 9 OF 18 MEDLINE
ACCESSION NUMBER: 2000063827 MEDLINE
DOCUMENT NUMBER: 20063827 PubMed ID: 10596003
TITLE: A word of caution in extrapolating the riluzole spinal cord injury protective effects obtained in a rabbit model under ketamine anesthesia.
COMMENT: Comment on: J Thorac Cardiovasc Surg. 1999 May;117(5):881-9
AUTHOR: Miyamoto T A; Miyamoto K J
SOURCE: JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY, (1999 Dec) 118 (6) 1156-7.
Journal code: 0376343. ISSN: 0022-5223.
PUB. COUNTRY: United States
Commentary
Letter
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000314
Entered Medline: 19991223
CT Check Tags: Animal
*Anesthetics, Dissociative: AD, administration & dosage
Cardiopulmonary Bypass: AE, adverse effects
Disease Models, Animal
Drug Synergism
Excitatory Amino Acid Antagonists: AD, administration & dosage
*Excitatory Amino Acid Antagonists: TU, therapeutic use
Follow-Up Studies
*Ischemia: PC, prevention & control
*Ketamine: AD, administration & dosage
Neurologic Examination
*Neuroprotective Agents: TU, therapeutic use
Rabbits
***Riluzole: TU, therapeutic use**
***Spinal Cord: BS, blood supply**
Spinal Cord: DE, drug effects
RN 1744-22-5 (Riluzole); 6740-88-1 (Ketamine)
CN 0 (Anesthetics, Dissociative); 0 (Excitatory Amino Acid Antagonists); 0 (Neuroprotective Agents)

L15 ANSWER 10 OF 18 MEDLINE

ACCESSION NUMBER: 2000009716 MEDLINE
DOCUMENT NUMBER: 20009716 PubMed ID: 10540024
TITLE: Prevention by insulin-like growth factor-I and riluzole in motor neuron death after neonatal axotomy.
AUTHOR: Iwasaki Y; Ikeda K
CORPORATE SOURCE: The Fourth Department of Internal Medicine, Toho University Ohashi Hospital, 2-17-6, Ohashi, Meguro-ku, Tokyo, Japan.
SOURCE: JOURNAL OF THE NEUROLOGICAL SCIENCES, (1999 Oct 31) 169 (1-2) 148-55.
Journal code: 0375403. ISSN: 0022-510X.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991202

AB Transection of the sciatic nerve in neonatal rats results discernable loss of motor neurons in the spinal cord. This neuronal death could be due to lack of retrogradely transported target derived neurotrophic factors, since some of these factors have been shown to be effective in injury induced motor neuron death. Another hypothesis suggests that glutamate and its receptors has been implicated as possible mechanism for motor neuron death, because inhibitor of glutamate release and antagonists of glutamate receptors are effective in preventing axotomized motor neuron death. To investigate the effect of insulin-like growth factor-I (IGF-I) and riluzole, a drug that inhibits glutamate release, on axotomy induced motor neuron death. Newborn rats were anesthetized with hypothermia. Sciatic nerve was cut near the obturator tendon in the left thigh. Animals were then treated daily with different doses of IGF-I and riluzole for 14 days with intraperitoneal injections. Control rats received PBS in the same fashion. After the treatment, the number of surviving motor neurons and the motor neuron diameter in the L(4) was assessed. Both IGF-I (1.0 mg/kg) and riluzole (5.0 mg/kg) rescued motor neuron death in a similar way. Co-administration of IGF-I (1.0 mg/kg) and riluzole (5.0 mg/kg) was more effective than either agent alone and there was a statistically significant difference between co-administration and IGF-I alone. However there was no significant difference between simultaneous treatment and riluzole alone. As for diameter of motor neurons, riluzole (5.0 mg/kg) preserved the motor neuron diameter in the lesion side. Nonetheless, no further increase in motor neuron diameter was seen when riluzole (5 mg/kg) and IGF-I (1.0 mg/kg) were applied in combination. Both agents did not affect diameter of motor neurons in the non-axotomy side. Riluzole is available in amyotrophic lateral sclerosis (ALS) and the positive results of clinical trials with IGF-I suggests that combination treatment of IGF-I and riluzole in ALS remains to be determined.

CT Check Tags: Animal
Animals, Newborn
Axotomy
Cell Death: DE, drug effects
Cell Death: PH, physiology
*Insulin-Like Growth Factor I: PD, pharmacology
*Motor Neurons: DE, drug effects
Motor Neurons: PH, physiology
*Neuroprotective Agents: PD, pharmacology
Rats

Rats, Sprague-Dawley
***Riluzole: PD, pharmacology**
Sciatic Nerve: DE, drug effects
Sciatic Nerve: PH, physiology
***Spinal Cord: DE, drug effects**
Spinal Cord: PH, physiology
RN 1744-22-5 (Riluzole); 67763-96-6 (Insulin-Like Growth Factor I)
CN 0 (Neuroprotective Agents)

L15 ANSWER 11 OF 18 MEDLINE
ACCESSION NUMBER: 1999424138 MEDLINE
DOCUMENT NUMBER: 99424138 PubMed ID: 10494351
TITLE: Neuroprotective effects of riluzole in neurotrauma models: a review.
AUTHOR: Wahl F; Stutzmann J M
CORPORATE SOURCE: Neurodegenerative Diseases Department, Rhone-Poulenc Rorer, CRVA, France.
SOURCE: ACTA NEUROCHIRURGICA. SUPPLEMENTUM, (1999) 73 103-10. Journal code: 0140560. ISSN: 0065-1419.
PUB. COUNTRY: Austria
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 19991101
Last Updated on STN: 19991101
Entered Medline: 19991020

AB Physical injury to the central nervous system (CNS) remains one of the main causes of mortality and disability in young adults. Numerous therapies have been successfully evaluated in experimental traumatic brain or spinal cord injuries (TBI, SCI) and, although some of them are currently under clinical trials for these indications, no drug therapy is at present available. Thus, an interesting approach to reduce the CNS injury-induced damage could be the blockade of Na(+)-channels by drugs such as riluzole which is neuroprotective in models of TBI or SCI as summarized in this review. Repeated doses ranging from 2 to 8 mg/kg were administered between 24 h to 10 days post-injury, with a first administration given either at 15 min or up to 6 h post-injury. In these models riluzole was found to reduce both the size of spinal cord and brain lesions as well as brain edema, and to restore the neurological, motor and cognitive impairments consequent of these injuries. The largest therapeutic time window obtained was 1 to 6 h in TBI. This such a compound should be considered as an interesting candidate for the treatment or SCI or TBI.

CT Check Tags: Animal
Brain Edema: DT, drug therapy
Brain Injuries: DI, diagnosis
*Brain Injuries: DT, drug therapy
Brain Injuries: PA, pathology
Brain Injuries: PP, physiopathology
Brain Injuries: PX, psychology
Cognition
Evoked Potentials, Somatosensory: DE, drug effects
Memory: DE, drug effects
Neurologic Examination
*Neuroprotective Agents: TU, therapeutic use
Rats

Rats, Sprague-Dawley
Rats, Wistar
***Riluzole: TU, therapeutic use**
***Spinal Cord Injuries: DT, drug therapy**
Spinal Cord Injuries: PA, pathology
Spinal Cord Injuries: PP, physiopathology
Wounds, Nonpenetrating: DI, diagnosis
Wounds, Nonpenetrating: DT, drug therapy
Wounds, Nonpenetrating: PA, pathology
Wounds, Nonpenetrating: PP, physiopathology
Wounds, Nonpenetrating: PX, psychology
RN 1744-22-5 (Riluzole)
CN 0 (Neuroprotective Agents)

L15 ANSWER 12 OF 18 MEDLINE
ACCESSION NUMBER: 1999238751 MEDLINE
DOCUMENT NUMBER: 99238751 PubMed ID: 10220679
TITLE: Riluzole prevents ischemic spinal cord injury caused by aortic crossclamping.
COMMENT: Comment in: J Thorac Cardiovasc Surg. 1999 Dec;118(6):1156-7
AUTHOR: Lang-Lazdunski L; Heurteaux C; Vaillant N; Widmann C; Lazdunski M
CORPORATE SOURCE: Department of Cardiovascular Surgery, Paris, and the Institute of Molecular and Cellular Pharmacology, Valbonne, France.
SOURCE: JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY, (1999 May) 117 (5) 881-9.
Journal code: 0376343. ISSN: 0022-5223.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990601
Last Updated on STN: 20000314
Entered Medline: 19990518

AB BACKGROUND: Recent studies support the involvement of glutamate neurotoxicity in the pathophysiology of spinal cord injury induced by aortic crossclamping. We investigated the effects of riluzole, a neuroprotective drug that blocks glutamatergic neurotransmission, in a rabbit model of spinal cord ischemia. METHODS: The infrarenal aortas of New Zealand White albino rabbits (n = 40) were occluded for 40 minutes. Experimental groups were as follows: sham operation group (n = 5), control group undergoing occlusion but receiving no pharmacologic intervention (n = 10), experimental group A (n = 10) receiving 8 mg/kg riluzole intravenously 30 minutes before ischemia, experimental group B (n = 10) receiving 4 mg/kg riluzole intravenously 30 minutes before ischemia and at the onset of reperfusion, and experimental group C (n = 10) receiving 8 mg/kg riluzole intravenously at the onset of reperfusion. Neurologic status was assessed at 6, 24, and 48 hours after the operation and then daily until the fifth day. All animals were killed at 24, 48, or 120 hours after the operation. Spinal cords were harvested for histopathologic studies, immunohistochemical studies for microtubule-associated protein 2, and search for morphologic features of apoptosis by the terminal deoxynucleotidyltransferase-mediated deoxyuridine triphosphate-biotin nick-end labeling staining method. RESULTS: All animals in the control

group became paraplegic. Except for 1 rabbit in group C, all riluzole-treated animals had better neurologic function. Luxol fast blue and terminal deoxynucleotidyltransferase-mediated deoxyuridine triphosphate-biotin nick-end labeling staining methods demonstrated typical morphologic changes characteristic of necrosis and apoptosis in control animals. Riluzole prevented or attenuated ischemia-induced necrosis, apoptosis, and cytoskeletal proteolysis, depending on the dose and the timing of administration. CONCLUSION: Riluzole may have therapeutic utility during high-risk operations on the thoracoabdominal aorta.

CT Check Tags: Animal; Comparative Study; Female; Support, Non-U.S. Gov't
Aorta, Abdominal: SU, surgery
Apoptosis: GE, genetics
Constriction
Cytoplasm: ME, metabolism
DNA: AN, analysis
DNA Fragmentation
Disease Models, Animal
Immunoenzyme Techniques
In Situ Nick-End Labeling
Injections, Intravenous
Ischemia: ME, metabolism
Ischemia: PA, pathology
*Ischemia: PC, prevention & control
Microtubule-Associated Proteins: ME, metabolism
Motor Neurons: DE, drug effects
Motor Neurons: ME, metabolism
Motor Neurons: PA, pathology
Necrosis
Neuroprotective Agents: AD, administration & dosage
*Neuroprotective Agents: TU, therapeutic use
Photomicrography
Rabbits
Riluzole: AD, administration & dosage
***Riluzole: TU, therapeutic use**
***Spinal Cord: BS, blood supply**
Spinal Cord: DE, drug effects
Spinal Cord: ME, metabolism

RN 1744-22-5 (Riluzole); 9007-49-2 (DNA)
CN 0 (Microtubule-Associated Proteins); 0 (Neuroprotective Agents)

L15 ANSWER 13 OF 18 MEDLINE
ACCESSION NUMBER: 1998163997 MEDLINE
DOCUMENT NUMBER: 98163997 PubMed ID: 9503266
TITLE: The glutamate antagonist riluzole suppresses intracortical facilitation.
AUTHOR: Liepert J; Schwenkreis P; Tegenthoff M; Malin J P
CORPORATE SOURCE: Department of Neurology, Ruhr University Bochum, Federal Republic of Germany.
SOURCE: JOURNAL OF NEURAL TRANSMISSION, (1997) 104 (11-12) 1207-14. Journal code: 9702341. ISSN: 0300-9564.
PUB. COUNTRY: Austria
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199804

ENTRY DATE: Entered STN: 19980507
Last Updated on STN: 19980507
Entered Medline: 19980429

AB The effect of the glutamate antagonist riluzole on excitatory and inhibitory phenomena in the human motor system was studied by transcranial magnetic stimulation (TMS) and peripheral electrical nerve stimulation. The motor threshold, the intracortical inhibition and intracortical facilitation as assessed by paired TMS, the cortical and peripheral silent periods, F wave amplitudes and F wave latencies were measured. Riluzole suppressed the intracortical facilitation whereas other parameters remained unchanged, indicating that the neurotransmitter glutamate is mainly involved in facilitatory mechanisms in the motor system.

CT Check Tags: Human
Adult
Cerebral Cortex: DE, drug effects
*Cerebral Cortex: PH, physiology
Electromagnetic Fields
Electrophysiology
Excitatory Amino Acid Antagonists: AE, adverse effects
*Excitatory Amino Acid Antagonists: PD, pharmacology
*Glutamic Acid: PH, physiology
Movement: DE, drug effects
Movement: PH, physiology
Peripheral Nervous System: DE, drug effects
Peripheral Nervous System: PH, physiology
Riluzole: AE, adverse effects
***Riluzole: PD, pharmacology**
Spinal Cord: DE, drug effects

RN 1744-22-5 (Riluzole); 56-86-0 (Glutamic Acid)

CN 0 (Excitatory Amino Acid Antagonists)

L15 ANSWER 14 OF 18 MEDLINE

ACCESSION NUMBER: 97465568 MEDLINE
DOCUMENT NUMBER: 97465568 PubMed ID: 9326288
TITLE: Rapid calpain I activation and cytoskeletal protein degradation following traumatic spinal cord injury: attenuation with riluzole pretreatment.
AUTHOR: Springer J E; Azbill R D; Kennedy S E; George J; Geddes J W
CORPORATE SOURCE: Department of Anatomy and Neurobiology, University of Kentucky Medical Center, Lexington 40536-0084, U.S.A.
CONTRACT NUMBER: AG-08974 (NIA)
NS-30248 (NINDS)
SOURCE: JOURNAL OF NEUROCHEMISTRY, (1997 Oct) 69 (4) 1592-600.
Journal code: 2985190R. ISSN: 0022-3042.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971027

AB Immunocytochemical and immunoblotting techniques were used to investigate calpain I activation and the stability of the calpain-sensitive cytoskeletal proteins microtubule-associated protein 2 (MAP2) and spectrin at 1, 4, and 24 h after contusion injury to the spinal cord. Spinal cord injury resulted in the activation of calpain I at all time points

examined, with the highest level of activation occurring at 1 h. At the same early time point, there was a loss of dendritic MAP2 staining in spinal cord sections, accompanied by pronounced perikaryal accumulation. The loss in MAP2 staining in the injured spinal cord progressed over the 24-h survival period to affect regions 3 mm distant to the site of injury. The presence of calpain I-specific spectrin degradation was apparent in neuronal cell bodies and fibers as early as 1 h after injury, with the most intense staining occurring within and juxtaposed to the injury site. Spectrin breakdown products in neuronal cell bodies declined rapidly at 4 h and were nearly undetectable at 24 h after injury. Immunoblot studies confirmed the immunocytochemical results by demonstrating a significant increase in calpain I activation, a significant decrease in MAP2 levels, and a significant increase in spectrin breakdown. Finally, treatment of animals with riluzole, an inhibitor of glutamate release, before surgery reduced significantly the loss of MAP2 levels observed at 24 h after injury. These results demonstrate that Ca2+-dependent protease activation and degradation of critical cytoskeletal proteins are early events after spinal cord injury and that treatments that minimize the actions of glutamate may limit their breakdown.

CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
*Calpain: ME, metabolism
*Contusions: ME, metabolism
*Cytoskeletal Proteins: ME, metabolism
Enzyme Activation
*Excitatory Amino Acid Antagonists: PD, pharmacology
Immunohistochemistry
Microtubule-Associated Proteins: ME, metabolism
Rats
***Riluzole: PD, pharmacology**
Spectrin: ME, metabolism
***Spinal Cord Injuries: ME, metabolism**

RN 12634-43-4 (Spectrin); 1744-22-5 (Riluzole)
CN 0 (Cytoskeletal Proteins); 0 (Excitatory Amino Acid Antagonists); 0 (Microtubule-Associated Proteins); EC 3.4.22.17 (Calpain)

L15 ANSWER 15 OF 18 MEDLINE
ACCESSION NUMBER: 97361683 MEDLINE
DOCUMENT NUMBER: 97361683 PubMed ID: 9218644
TITLE: Riluzole promotes survival of rat motoneurons in vitro by stimulating trophic activity produced by spinal astrocyte monolayers.
AUTHOR: Peluffo H; Estevez A; Barbeito L; Stutzmann J M
CORPORATE SOURCE: Instituto Clemente Estable and Facultad de Ciencias, Montevideo, Uruguay.
SOURCE: NEUROSCIENCE LETTERS, (1997 Jun 13) 228 (3) 207-11. Journal code: 7600130. ISSN: 0304-3940.
PUB. COUNTRY: Ireland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 19970916
Last Updated on STN: 19980206
Entered Medline: 19970902

AB In the present study we have assessed whether riluzole stimulates the production of trophic activities for motoneurons by spinal astrocyte cultures. Astrocyte monolayers prepared from new-born rats were exposed to

vehicle or riluzole (1-10 microM) for 30-36 h, then washed and further incubated without riluzole for 24 h in L15 medium to obtain the astrocyte conditioned media (ACM). Motoneuron-enriched cultures were used to test the ability of the ACM to support motoneuron viability. Astrocyte monolayers exposed to 1 microM riluzole did not show changes in morphology or in DNA or protein synthesis. However, the conditioned medium obtained from astrocyte monolayers after this treatment increased motoneuron survival compared to that from vehicle-treated cultures. A similar effect was found when astrocytes were exposed to a higher riluzole concentration (10 microM) but with greater dilutions of the conditioned medium. This trophic activity was abolished by boiling or after treatment with trypsin. These findings strongly suggest the existence of a new trophic mechanism, through which riluzole may exert motoneuron protection.

CT Check Tags: Animal
*Astrocytes: DE, drug effects
Cell Survival: DE, drug effects
Cells, Cultured
Culture Media, Conditioned
DNA: BI, biosynthesis
Immunohistochemistry
Leucine: ME, metabolism
*Motor Neurons: DE, drug effects
Nerve Tissue Proteins: BI, biosynthesis
*Neuroprotective Agents: PD, pharmacology
Rats
Receptors, Nerve Growth Factor: BI, biosynthesis
Riluzole
***Spinal Cord: CY, cytology**
Spinal Cord: DE, drug effects
*Thiazoles: PD, pharmacology
Thymidine: ME, metabolism

RN 1744-22-5 (Riluzole); 50-89-5 (Thymidine); 61-90-5 (Leucine); 9007-49-2 (DNA)

CN 0 (Culture Media, Conditioned); 0 (Nerve Tissue Proteins); 0 (Neuroprotective Agents); 0 (Receptors, Nerve Growth Factor); 0 (Thiazoles)

L15 ANSWER 16 OF 18 MEDLINE

ACCESSION NUMBER: 96290627 MEDLINE
DOCUMENT NUMBER: 96290627 PubMed ID: 8730788
TITLE: The effect of riluzole on post-traumatic spinal cord injury in the rat.
AUTHOR: Stutzmann J M; Pratt J; Boraud T; Gross C
CORPORATE SOURCE: Neurodegenerative Diseases Department, Rhine-Poulenc Rorer, CRVA, Vitry, France.
SOURCE: NEUROREPORT, (1996 Jan 31) 7 (2) 387-92.
Journal code: 9100935. ISSN: 0959-4965.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199611
ENTRY DATE: Entered STN: 19961219
Last Updated on STN: 19980206
Entered Medline: 19961125

AB This study evaluated treatment with riluzole, a neuroprotective agent, following thoracic spinal cord compression in the rat. Animals received

riluzole (2 mg kg-1) or vehicle twice daily for 10 days following the trauma. Motor deficits, somatosensory evoked potentials (SEP) and lesion histology were evaluated. Although paralysis was seen following trauma, seven of 10 animals receiving riluzole recovered motor function and nearly normal behaviour, unlike animals receiving vehicle. Trauma dramatically disturbed SEPs with falls in amplitude and increases in latency. After riluzole SEP returned towards pre-injury levels, while untreated animals showed no recovery. Morphological studies revealed significant (53%) reduction in the degree of spinal cord infarcted after riluzole treatment.

CT Check Tags: Animal; Male
Anesthesia
Evoked Potentials, Somatosensory: DE, drug effects
Hemorrhage: PP, physiopathology
*Neuroprotective Agents: TU, therapeutic use
Paralysis: DT, drug therapy
Paralysis: PP, physiopathology
Rats
Rats, Wistar
Riluzole
Spinal Cord: PA, pathology
***Spinal Cord Compression: DT, drug therapy**
Spinal Cord Compression: PA, pathology
Spinal Cord Compression: PP, physiopathology
*Thiazoles: TU, therapeutic use
Time Factors
RN 1744-22-5 (Riluzole)
CN 0 (Neuroprotective Agents); 0 (Thiazoles)

L15 ANSWER 17 OF 18 MEDLINE
ACCESSION NUMBER: 96197937 MEDLINE
DOCUMENT NUMBER: 96197937 PubMed ID: 8967745
TITLE: Benefit of vitamin E, riluzole, and gabapentin in a transgenic model of familial amyotrophic lateral sclerosis.
COMMENT: Comment in: Ann Neurol. 1996 Feb;39(2):145-6
AUTHOR: Gurney M E; Cutting F B; Zhai P; Doble A; Taylor C P; Andrus P K; Hall E D
CORPORATE SOURCE: Department of Cell and Molecular Biology, Northwestern University Medical School, Chicago, IL, USA.
SOURCE: ANNALS OF NEUROLOGY, (1996 Feb) 39 (2) 147-57. Journal code: 7707449. ISSN: 0364-5134.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19980206
Entered Medline: 19961212

AB Familial amyotrophic lateral sclerosis (FALS) has been linked in some families to dominant mutations of the SOD1 gene encoding Cu,Zn superoxide dismutase (Cu,ZnSOD). We have used a transgenic model of FALS based on expression of mutant human Cu,ZnSOD to explore the etiology and therapy of the genetic disease. Expression of mutant, but not wild-type, human Cu,ZnSOD in mice places the brain and spinal cord under oxidative stress. This causes depletion of vitamin E, rather than the typical age-dependent increase in vitamin E content as occurs in nontransgenic mice and in mice expressing wild-type human Cu,ZnSOD. Dietary supplementation with vitamin

E delays onset of clinical disease and slows progression in the transgenic model but does not prolong survival. In contrast, two putative inhibitors of the glutamatergic system, riluzole and gabapentin, prolong survival. However, riluzole did not delay disease onset. Thus, there was clear separation of effects on onset, progression, and survival by the three therapeutics tested. This suggests the hypothesis that oxidative damage produced by the expression of mutant Cu,ZnSOD causes slow or weak excitotoxicity that can be inhibited in part by alerting glutamate release or biosynthesis presynaptically.

CT Check Tags: Animal; Human
*Acetic Acids: TU, therapeutic use
Amyotrophic Lateral Sclerosis: DT, drug therapy
*Amyotrophic Lateral Sclerosis: GE, genetics
Amyotrophic Lateral Sclerosis: ME, metabolism
Brain: ME, metabolism
Diet
Disease Progression
Mice
Mice, Transgenic
Oxidative Stress
Riluzole
Spinal Cord: ME, metabolism
Superoxide Dismutase: GE, genetics
Survival Analysis
*Thiazoles: TU, therapeutic use
Vitamin E: AD, administration & dosage
*Vitamin E: TU, therapeutic use

RN 1406-18-4 (Vitamin E); 1744-22-5 (Riluzole); 60142-96-3 (gabapentin)
CN 0 (Acetic Acids); 0 (Thiazoles); EC 1.15.1.1 (Superoxide Dismutase)

L15 ANSWER 18 OF 18 MEDLINE
ACCESSION NUMBER: 90374172 MEDLINE
DOCUMENT NUMBER: 90374172 PubMed ID: 1975768
TITLE: In vivo evidence for an inhibitory glutamatergic control of serotonin release in the cat caudate nucleus: involvement of GABA neurons.
AUTHOR: Becquet D; Faudon M; Héry F
CORPORATE SOURCE: Laboratoire de Neuroendocrinologie Experimentale, Faculte de Medecine Nord, I.N.S.E.R.M. U.297, Marseille, France.
SOURCE: BRAIN RESEARCH, (1990 Jun 11) 519 (1-2) 82-8.
Journal code: 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199010
ENTRY DATE: Entered STN: 19901122
Last Updated on STN: 19980206
Entered Medline: 19901016

AB The local effect of L-glutamic acid (5 x 10(-5) M) on the release of [3H]serotonin continuously synthesized from [3H]tryptophan was examined in the caudate nucleus of 'encephale isole' unanaesthetized cats implanted with push-pull cannula. L-Glutamic acid (5 x 10(-5) M) decreased [3H]serotonin release from nerve terminals of the dorsalis raphe-striatal serotonergic neurons. The effect was antagonized by 2-amino-6-trifluoromethoxybenzothiazole (PK 26124) (10(-6) M), an antagonist of glutamatergic transmission. This effect was mimicked by

N-methoxy-D-aspartic acid NMDA (5 x 10(-5) M) and prevented by DL-2-phosphono-valeric acid (APV) (5 x 10(-6) M), indicating that L-glutamic acid decreased serotonin release via a N-methoxy-D-aspartate type receptor. The superfusion of serotonergic nerve terminals in the caudate nucleus with tetrodotoxin prevented the inhibitory L-glutamic acid-induced effect on serotonin release. Furthermore, L-glutamic acid-induced inhibition of [3H]serotonin release was antagonized by bicuculline (5 x 10(-5) M). These data suggest that the glutamatergic receptors involved were not located directly on serotonin nerve terminals. The inhibitory control exerted by L-glutamic acid on serotonergic transmission could involve gamma-aminobutyric acid interneurons. Since no reduction of spontaneous [3H]serotonin release was observed in the presence of bicuculline, GABAergic neurons appeared to exert a phasic influence on serotonin release. Indirect inhibitory presynaptic control on serotonin release mediated by corticostriatal glutamatergic fibers is discussed in light of previous findings.

CT Check Tags: Animal; Female; Male
2-Amino-5-phosphonovalerate: PD, pharmacology
Aspartic Acid: AA, analogs & derivatives
Aspartic Acid: PD, pharmacology
Bicuculline: PD, pharmacology
Cats
Caudate Nucleus: DE, drug effects
*Caudate Nucleus: PH, physiology
Glutamates: PD, pharmacology
*Glutamates: PH, physiology
Glutamic Acid
N-Methylaspartate
Neurons: DE, drug effects
*Neurons: PH, physiology
Riluzole
*Serotonin: SE, secretion
Spinal Cord: PH, physiology
Synaptic Transmission: DE, drug effects
Tetrodotoxin: PD, pharmacology
Thiazoles: PD, pharmacology
*gamma-Aminobutyric Acid: PH, physiology

RN 1744-22-5 (Riluzole); 4368-28-9 (Tetrodotoxin); 485-49-4 (Bicuculline); 50-67-9 (Serotonin); 56-12-2 (gamma-Aminobutyric Acid); 56-84-8 (Aspartic Acid); 56-86-0 (Glutamic Acid); 6384-92-5 (N-Methylaspartate); 76726-92-6 (2-Amino-5-phosphonovalerate)

CN 0 (Glutamates); 0 (Thiazoles)